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(54) Title: ADMINISTRATION OF BIOLOGICALLY ACTIVE MATERIAL

(57) Abstract

A living organism having a cuticular covering is administered with biologically active material in admixture with amorphous powdered silica, so as to disrupt the cuticular covering and permit the biologically active material to pass through the covering. The biologically active material may be a weedkiller or insecticide.

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# Administration of Biologically Active Material

The present invention relates to a method of administering a biologically active material to a living organism having a cuticular covering, such as weed or insect.

Hormonal weedkillers are typically selective for broad leaved dicotyledonous species of weeds. Grasses or the like are monocotyledonous and therefore are not significantly affected by the action of such weedkillers. Typically application of recommended doses of such weedkillers results in penetration of the waxy protective outer layer of the cuticle, and consequent entry into the plant tissue causing aberrant growth of the weed. The weed should therefore, in theory, become exhausted and die. However, in practice it is often necessary to apply the weedkiller; repeatedly total eradication of the weed is rarely achieved.

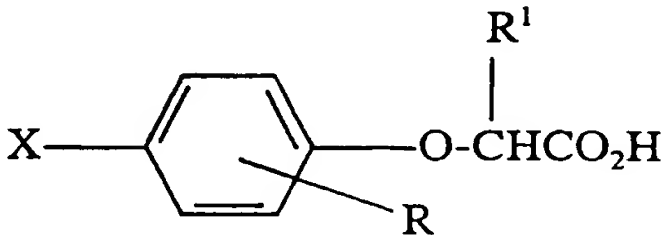
Contact insecticides act in a similar manner; they penetrate the target insect cuticle by reason of their solubility in the waxy protective outer layer of the cuticle. The insecticides enter the insect's body and disrupt nervous or other metabolic functions resulting in death of the insect. Such penetration may, however, not be highly efficient.

It is therefore an object of the present invention to alleviate such difficulties and to provide weedkiller and insecticide formulations which are of substantially increased effectiveness.

Thus, according to the present invention, there is provided a method of administering a biologically active material to a living organism having a cuticular covering, which method comprises administering a mixture of amorphous, powdered silica and the biologically active material so as to interfere with the integrity of the waxy outer layer of the cuticular covering and permit the biologically active material to pass through the covering. Desirably, the biologically active material is one which kills the organism.

According to a first aspect of the present invention the living organism is a weed.

Typically, the biologically active material comprises at least one compound of the Formula I, together with a carrier



(I)

where X is a halogen atom and R is either halogen or a lower alkyl group and $R^1$ is either hydrogen or a lower alkyl group.

Preferably, the biologically active material contains two compounds of Formula I, the compounds being 2-(4-dichlorophenoxy) acetic acid and 2-(4-chloro-o-tolyloxy) propionic acid.

These compounds are known to be selective weedkillers; a formulation containing the two compounds is commercially available under the trade mark SUPERTOX™. The addition of silicon dioxide to such a known formulation results in a surprising synergistic effect which advantageously is selective for broad leaved dicotyledonous weed species, and furthermore has no visible effect on the grasses or other monocotyledonous plants.

Preferably, the carrier is aqueous, more preferably substantially pure water. In one embodiment of the first aspect of the present invention the silicon dioxide may be synthetic amorphous silicon dioxide; the silicon dioxide may be substantially anhydrous until mixed with the carrier.

According to a second aspect of the present invention the living organism is an insect.

Typically, the biologically active material comprises deltamethrin, triflumuron or a fungus.

Preferably, when the living organism is a fungus, the fungus comprises *Beauvaria bassiana*.

The invention may be more clearly understood from the following illustrative examples.

Example 1

Six trays each of 20 daisies (3 weeks post transplant) were treated as follows:

i) 20ml of synthetic amorphous silicon dioxide in 1 litre of water was applied to two daisy trays as a control;

ii) 25ml of the Supertox formulation in 1 litre of water was applied to two trays of daisies;

iii) 25ml of Supertox in 1 litre of water plus 20ml of synthetic amorphous silicon dioxide was applied to two trays of daisies.

The soil in the trays was watered daily and placed in a randomised design in the glasshouse.

The results of the experiment after three weeks showed that the formulation comprising both Supertox and the silicon dioxide was highly selective for the daisies, and were as follows:

i) The control application of silicon dioxide alone had no effect on the daisies;

ii) The Supertox weedkiller used alone resulted in recovery of the daisies;

iii) The combined formulation of silicon dioxide and Supertox completely eradicated the daisies.

Further application of the combined formulation to daisies on a lawn resulted in no destruction of the grasses, which were visibly unharmed.

Example 2

Eight plots (each ca. 10 $m^{-2}$) were marked out on an area of unmown grass and broadleaf weeds. Two control plots had 4.5L of water applied utilising a hydraulic knapsack sprayer. 30ml

of silica dust (Gasil 23D) was applied in 4.5L of water to each of two randomly selected plots. The two other randomly allocated treatments were as follows:

20ml of Verdone 2 (2 plots)

30ml of Gasil 23D + 20ml of Verdone 2 (2 plots)

The application of the Verdone 2 at this rate is half the recommended dose according to the label. The plant species present in the plots were recorded prior to treatment. The plots were left, and watered only by natural rainfall and examined after 4 weeks.

i) The control application of silicon dioxide alone had no effect on the broadleaf weeds:

ii) The application at half the recommended rate of Verdone 2 caused a delay in the flowering of the broadleaf weeds, but did not kill these;

iii) The control formulation of silicon dioxide and Verdone 2 caused the death of the following weed species:

*Sonchus arvensis*
*Stellaria media*
*Bellis perennis*
*Taraxacum officinale*
*Medicago lupulina*
*Senecio yacobeae*
*Rannunculus bulbosus*

The silica dust alone or in combination with the Verdone 2 caused no visible harm to the grasses.

Example 3

*Beauvaria bassiana* is an entomopathogenic fungus, that requires relatively high humidity in order to germinate and penetrate an insect cuticle. Under conditions of 70% RH *Beauvaria bassiana* was tested alone and in combination with silicon dioxide (Gasil 23D), applied to filter paper and presented to the blood sucking bugs *Rhodnius prolixus*. This continuous exposure experiment conducted on 30 individual bugs produced the following results:

At 22 days mortality of 1st instar *Rhodnius* individuals treated with *B. bassiana* alone was 50% while with *B. bassiana* and silicon dioxide in combination mortality was 70% over the same period.

*B. bassiana* was applied to the insect perches at a rate of $2.3 \times 10^5$ conidia and 5mg of silicon dioxide per ml water and applied to the insect perches.

Example 4

Triflumuron is an insect growth regulator which inhibits insect moults between different instars. Normally, adsorption through the cuticle is inefficient with triflumuron, but with the addition of silicon dioxide triflumuron may enter via the cuticle more easily and influence development of the insects.

Triflumuron was used at 1% concentration alone and in combination with 15g/litre of Dri-die (silicon dioxide) applied to filter paper perches for the bugs *Rhodnius prolixus*.

The addition of the silica to the triflumuron treated targets resulted in increased deaths of the insects with continuous tarsal contact for 21 days.

With triflumuron alone 30% deaths were recorded due to unsuccessful moults. With the addition of silica dust 60% of deaths were caused by unsuccessful moults (defined by splitting of the cuticle of the abdomen) while an additional 30% of deaths were caused by other means.

Example 5

Silicon dioxide aerogel, Gasil 23D, kills houseflies which come into contact with it by the disruption of the integrity of the cuticle permitting water loss and hence desiccation of the insect. To test its effect against terrestrial invertebrates other than insects ten woodlice were placed in each of two plastic dishes and a filter paper placed on the bottom of each to act as a shelter. In one dish

a sprinkling of silica dust (Gasil 23D) was placed around the inside bottom rim such that isopods would make contact as they walked around the bottom of the dish. The other dish was left as a control. After 24 hours one woodlouse was dead in the control dish and six were dead in the experimental. After 48 hours nine were dead in the control and all ten were dead in the experimental. It was therefore concluded that the silica dust accelerated the rate of water loss in the experimental woodlice.

Example 6

Silicon dioxide aerogel, Gasil 23D, prolongs the activity of a synthetic pyrethroid insecticide, namely deltamethrin, when used by contact with the American cockroach, *Periplameta Americana*.

The combination also produces the same mortality effects as a higher dose of insecticide used without the silicon dioxide adjuvant.

Example 7

An area of waste ground was divided into three plots each measuring approx 3m x 3m. The plots, on each of which the vegetation was predominantly grasses and perennial broadleaf weeds, were sprayed (using a hand sprayer) with an aqueous liquid so as to lightly wet the leaves of the vegetation. The aqueous liquids used were as follows:

Plot 1 500 ml of water only (control);

Plot 2 15 ml of a commercially available glyphosate weedkiller, commercially available under the trade mark Roundup GC Biactive, in 500 ml of water; and

Plot 3 As for Plot 2, with the addition of 0.76g amorphous silicon dioxide.

The plots were then observed over a three week period, during which the prevailing weather was mostly dry and warm, with approximately four wet days (including some heavy showers and thunderstorms).

In the control plot (Plot 1), very little change was noted after two or three weeks.

In Plot 2, there was a large proportion of dead or dying vegetation after two weeks, although some tufts of grass were still green and alive. In particular, a clump of tubular-leaved "bog grass" was surviving. After three weeks, the majority of the grass remained either dead or dying; however, the "bog grass" continued to survive.

In Plot 3, all the vegetation was either dead or dying after two weeks, with all the vegetation (including the "bog grass") being dead after three weeks.

This test shows that the silica can improve the performance of a glyphosate weedkiller, both in terms of speed and the ability to kill difficult weeds.

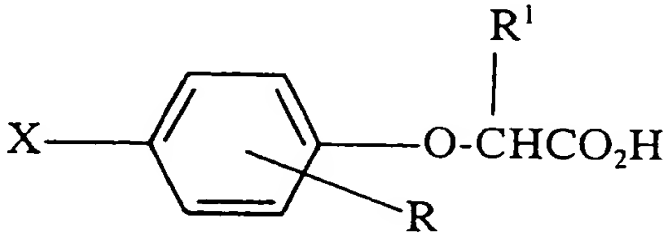
**CLAIMS:**

1. A method of administering a biologically active material to a living organism having a cuticular covering, which method comprises administering a mixture of amorphous powdered silica and said biologically active material so as to disrupt said cuticular covering and permit said biologically active material to pass through said covering.

2. A method according to claim 1, wherein said biologically active material kills said living organism.

3. A method according to claim 1 or 2, wherein said living organism is a weed.

4. A method according to claim 3, wherein said biologically active material comprises at least one compound of the formula I, together with a carrier,




(I)

where X is a halogen atom and R is either halogen or a lower alkyl group and $R^1$ is either hydrogen or a lower alkyl group.

5. A method according to claim 3 or 4, wherein said biologically active material contains two compounds of said formula I, said compounds being 2-(dichlorophenoxy) acetic acid and 2-(4-chloro-o-tolyoxy) propionic acid.

6. A method according to any of claims 3 to 5, wherein said carrier is aqueous.

7. A method according to any of claims 3 to 6, wherein said carrier is substantially pure water.

8. A method according to any of claims 3 to 7, wherein said silicon dioxide is substantially anhydrous until mixed with said carrier.

9. A method according to claim 1 or 2, wherein said living organism is an insect.

10. A method according to claim 9, wherein said biologically active material comprises deltamethrin.

11. A method according to claim 9, wherein said biologically active material comprises triflumuron.

12. A method according to claim 9, wherein said biologically active material comprises a fungus.

13. A method according to claim 12, wherein said fungus comprises *Beauvaria bassiana*.

14. A method of administering a biologically active material to a living organism having a cuticular covering, substantially as described herein with reference to the Examples.

# INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A01N25/00 A01N25/08 A01N59/00 //(A01N59/00,57:20,63:04, 53:00,47:34,39:04,39:02,61:00)

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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| X,P | WO,A,96 05721 (MOSANTO COMPANY) 29 February 1996<br>see page 1, line 1-20<br>see page 12, line 28 - line 35<br>see page 13, line 25 - line 38<br>see page 14, line 25 - line 36<br>see page 18, line 32 - page 19, line 7<br>see page 19, line 38 - page 20, line 3<br>see page 20, line 31 - line 34<br>see page 23, line 12 - page 24, line 15<br>see examples 1-51<br>---<br>-/-- | 1-8 |

[X] Further documents are listed in the continuation of box C.

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